REMARKS

Applicant thanks the Examiner for the careful consideration given to the subject action. The detailed nature of the December 24, 2008 Office Action provided considerable assistance in preparing this response. This response will address each of the issues raised in the Office Action in the order in which they were raised.

Priority

In the December 24, 2009 Office Action, the Examiner asserts certain claims of the subject application are not entitled to claim the benefit of the filing date of Application Serial No. 60/065,825 filed on November 14, 1997 because that application "fails to provide explicit or implicit descriptive support for a nonhuman mammal whose germ cell comprises lentiviral vector as recited in claims 183-186, 189-196, 199-205, 208-210 and 211 of this application." The Examiner invited applicants to indicate the page and line numbers for such written support in the '825 application.

Before doing so, it is important to note that lentiviral vectors are a type of retrovirus that can infect both dividing and non-dividing cells because their pre-integration complex (virus "shell") can get through the intact membrane of the nucleus of the target cell. One example is HIV. HIV is the type of lentiviral vector disclosed in U.S. Patent No. 6,316,692 from

which the subject application is a divisional. HIV is the type of lentiviral vector discussed in U.S. Patent No. 6,156,952 to Bryant et al which is the basis for the rejection of certain claims made by the Examiner in the December 24, 2008 Office Action. More to the point, the use of HIV vectors is discussed in the '825 application filed November 14, 1997, approximately five months before the filing date of the Bryant et al application cited by the Examiner.

Turning then to the disclosure of the '825 application and the support it provides for "a nonhuman mammal whose germ cell comprises lentiviral vector", page 3 at lines 20-26 states: "This invention relies on the fact that vast numbers of male germ cells are more readily available." This same paragraph references mice which are non-human mammals. Elsewhere, the '825 application discusses use of various non-human mammals including "non-human primates, for example simians, marmosets, domestic agricultural animals such as sheep, cows, pigs, horses, particularly race horses, marine mammals, feral animals, rodents such as mice and rats, and the like." See page 11, lines 20-25. Page 15 at lines 1-13 discusses the manner in which germ cells may be extracted from such animals and stored.

At page 10, lines 15-23, the '825 application provides examples of viruses suitable for use in carrying out the invention. "Examples of viruses which are suitable for use

herein are adenoviruses, adeno-associated viruses, retroviruses such human immune-deficiency virus, mumps virus, and tranfecting fragments thereof, and other viral DNA segments..." (emphasis added). The '825 application further states in this same paragraph: "All of the above virus may require modification to render them non-pathogenic or less antigenic. Other known systems, however, may also be utilized within the confines of the invention." As noted above, lentiviral vectors are a type of retrovirus and HIV (human immune deficiency virus) is an example of such a lentiviral vector. Further, at page 26, lines 1-18, the '825 application describes a method involving the use of a transfecting agent comprising a viral vector selected from a group including retroviral vectors. Specific reference is made to human immunodeficiency vectors. At page 34, line 20 - page 35, line 23 another method is described using a transferring agent which comprises a viral vector selected from a group including retroviral vectors and human immunodeficiency vectors.

As noted above, lentiviral vectors are a category of retroviral vectors and human immunodeficiency vectors are a category of lentiviral vectors. As such, the '825 application provides explicit and implicit descriptive support for a non-human mammal whose germ cell comprises lentiviral vector. The '825 application provides explicit support for at least a non-human mammal whose germ cell comprises human immunodeficiency

vectors which are lentiviral vectors and at least implicit support for a non-human mammal whose germ cell comprises other lentiviral vectors when it references retroviral vectors and gives an example of at least one (HIV) which is also a lentiviral vector.

Claim Rejections 35 USC § 112

In the December 24, 2008 Office Action, the Examiner withdrew the prior objections raised under 35 USC § 112, but interposed a new rejection relating to claims 193-196, 199-205, 208-210 and 211. Specifically, the Examiner stated the specification "does not reasonably provide enablement for transplanting germ cell from one species of mammal to the testis of different species of mammal or interspecies xenogenic transplant to produce transgenic nonhuman mammal or a progeny thereof." The Examiner continued: "The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims." This rejection is respectfully traversed.

The enablement requirement of 35 USC § 112, paragraph 1 does not require every mode of making and using the invention be described in the specification. "The enablement requirement is met if the description enables any mode of making and using the claimed invention." *Engel Industries, Inc. v. Lockformer Co.*,

946 F.2d 1528, 20 USPQ 29 1300 (Fed. Cir. 1991). Further, the patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention so long as such experimentation is not unreasonable or undue. See *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 52 USPQ 2d 1129 (Fed. Cir. 1999). As noted in *Enzo*, supra, eight factors are typically considered. These include:

(1) the quantity of experimentation necessary;

(2) the amount of direction and guidance presented;

(3) the presence or absence of working examples;

(4) the nature of the invention;

(5) the state of the prior art;

(6) the relative skill of those in the art;

(7) the predictability or unpredictability of the art; and

(8) the breadth of the claims.

Of the claims which are the subject of the rejection, only claims 193 and 203 are written in independent form. Claims 193 and 203 will be the primary focus of this discussion, since they are the broadest of the claims which are the subject of the rejection.

As the Examiner acknowledged in the first paragraph of page 4 of the Office Action, claim 193 is fully enable by the specification for allogeneic donor male non-human mammals. The

claim covers the use of allogeneic donors. The claim, therefore, meets the *Engel Industries'* test set forth above. The description clearly enables a mode of making and using the claimed invention. The Examiner's comments suggest he may be under the impression that interspecies germ cell translation is occurring such that one species produces offspring of a different species. This is incorrect. The male germ cell of the host animal is being transfected with a polynucleatide not normally found in that germ cell. This is not interspecies germ cell transplantation. The kind of change occurring is the inclusion of e.g., a marker protein such as GFP into the germ cell so that offspring of the same species are produced expressing that gene. In the case of GFP, the offspring will fluoresce. Based on applicant's disclosure, one skilled in the art would be able to practice the invention using either an allogeneic host as the Examiner acknowledged or a non-allogeneic host without undue or unreasonable experimentation.

With respect to claim 203, the Examiner acknowledged in the second paragraph on page 4 of the Office Action that claim 203 is fully enabled by the specification if the male germ cell is obtained from an allogeneic non-human mammal. Under the *Engel Industries'* test this is all that is required to satisfy the enablement requirement because claim 203 does not distinguish between obtaining the male germ cell from an allogeneic or non-

allogeneic non-human mammal. Further, given the nature of the invention, the detailed nature of the disclosure and the level of skill in the art, one of ordinary skill would be able to practice the invention with germ cells from an allogeneic non-human mammal as acknowledged by the Examiner or using germ cells from a non-allogeneic non-human mammal without undue or unreasonable experimentation.

For these reasons, applicant respectfully requests the rejection of claims 193-196, 199-205, 208-210 and 211 be withdrawn.

Claim Rejections 35 USC § 102

In the December 24, 2008 Office Action the Examiner withdrew certain rejections previously imposed under 35 USC § 102(e) based on U.S. Patent No. 6,156,952 to Bryant et al and an article authored by Leonard et al. However, the Examiner rejected claims 185-186, 195-196, 203-205, 208-210 and 211 under 35 USC § 102(e) based on U.S. Patent No. 6,156,952 to Bryant et al.

Applicant respectfully submits any rejection of the claims based on the Bryant et al patent is erroneous and should be withdrawn given the discussion provided above under the heading "Priority". The claims in question of the subject application should be afforded priority as of November 14, 1997 which predates the filing date to the Bryant et al application by approximately five months. Further, in rejecting the claims the

Examiner states Bryant et al teaches transgenic non-human animal whose genome comprises lentiviral (e.g., HIV). The '825 application specifically teaches the use of a transfecting agent comprising HIV vectors and thus transgenic non-human animal whose genome comprises lentiviral, specifically HIV. Under such circumstances, 35 USC § 102(e) does not serve as a proper statutory basis for rejection of applicant's claims.

Even if the application for the Bryant et al patent was early enough to be prior art, a reading of Bryant et al indicates they are studying expression activity of different portions of the HIV genome as a method for understanding the virus and its mode of action. Bryant et al are generating transgenic mice by using the classic method of injection of the gene construct into the fertilized egg as opposed to the transduction of male germ cells as required by the claims of the present invention. Therefore, the method of Bryant et al is different from that of the present invention and the immediate product of the process is also different, as the product of the current invention is a transduced male germ cell that may then be subsequently used to produce a transgenic animal. Thus, the claimed and Bryant et al products are not identical or substantially identical in structure or composition and they are certainly not produced by identical or substantially identical processes.

In view of the foregoing, applicant respectfully requests the rejection under 35 USC § 102(e) be withdrawn.

Claim Rejections 35 USC § 103

In the December 24, 2008 Office Action the Examiner rejected all of the pending claims under 35 USC § 103 as being unpatentable over Brinster et al (U.S. Patent No. 5,858,354) and the 1996 Naldini et al article. Again, this rejection is respectfully traversed.

At page 14 of the Office Action, the Examiner acknowledges Brinster et al do not specifically disclose lentiviral vectors. To attempt to address this deficiency, the Examiner cites Naldini. While Naldini does describe lentiviral vectors, it does not provide any suggestion or teaching of the use of lentiviral vectors required by applicant's claims. Naldini only describes using lentiviral vectors in the transfection of adult rat brains. There is no suggestion of the lentiviral vector of Naldini being suitable for transfection of male germ cells. It is difficult to transfect male germ cells and nothing in either Naldini or Brinster et al suggests to one of ordinary skill in the art the use of lentiviral vectors would work. This combination of references teaches away from such use of lentiviral vectors because Brinster describes other vectors that do work. Given Brinster's description of other vectors that do work, there is nothing in either Naldini or Brinster that would motivate one of

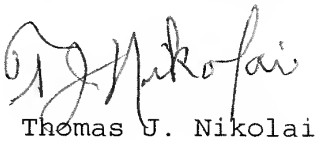
ordinary skill to use lentiviral vectors that may not work. Only through the impermissible application of hindsight based on applicant's disclosure would one think to use a lentiviral vector as a substitute for the vectors described in Brinster.

In view of the foregoing, applicant submits the rejection under 35 USC § 103 is improper and should be withdrawn.

For the reasons advanced, then, claims 183-186, 189-196, 199-205 and 208-211 are in condition for allowance and a notice to that effect is respectfully requested.

Respectfully submitted,

NIKOLAI & MERSEREAU, P.A.



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